

EXAMINER'S REMARKS

In the Office Action mailed October 22, 2002, claims 1-5 and 11-19 were pending. The Examiner rejected these same claims. Applicants address the Examiner's rejections in the same order these same rejections were set out in the Office Action mailed October 22, 2002.

1. The Examiner acknowledges Applicants' election of claims 1-5 and 11-19.
2. The Examiner acknowledges receipt of Applicants' Information Disclosure Statement.
3. The Examiner objects to informalities in the Declarations originally filed with the application.
4. The Examiner rejects Claims 1-5 and Claims 11-19 under 35 U.S.C. §112, second paragraph.

APPLICANTS' REMARKS

1. Withdrawn Claims

Applicants acknowledge the withdrawal of claims 6-10, from the prosecution of the instant application, consistent with the Election as filed on July 15, 2002.

2. Information Disclosure Statement

Applicants acknowledge the Examiner's entry of the Information Disclosure Statement filed on April 4, 2001.

3. Applicants File New Declarations

Applicants attach, herewith, a new set of executed Declarations from each of the named inventors. Specifically, these new Declarations make a priority claim under 35 U.S.C. §119(e) and, thereby, traverse the Examiner's objection to the Declarations attached to the application as filed.

4. The Claims Are Definite

Claims 1-5 and 11-19 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Federal Circuit case law (and the MPEP) make it clear that the definiteness of claim language must be analyzed, not in a vacuum, but in light of: 1) the content of the particular application's disclosure; 2) the teachings of the prior art; and 3) the claim interpretation that would be given by one possessing the ordinary level of skill in the art at the time the invention was made. (MPEP § 2173.02). See also *In re Marosi*, 218 USPQ 289 (Fed. Cir. 1983); *Rosemount, Inc. v. Beckman Instruments, Inc.*, 221 USPQ 1 (Fed. Cir. 1984); and *W.L. Gore & Associates, Inc. v. Garlock, Inc.* 220 USPQ 303 (Fed. Cir. 1983). In view of the authority cited above, Applicants submit the pending claims are definite.

A. A "Method" Is An Acceptable Preamble

The Examiner states that (for claims 1-5 and 11-19):

"[e]ach of the claimed methods is vague and indefinite in that there is no stated outcome for the methods in the preamble of the claims. The preamble merely states the works 'A method' or 'The method', followed by methods steps. This makes it impossible for one to determine whether one has

successfully preformed the claimed method as there is no stated end result. It would be remedial to amend the claim language to clearly state the intended outcome of the claimed method."¹

Applicants respectfully disagree. However, in order to further their business interests and without acquiescing to the Examiner's arguments, while expressly reserving the right to prosecute the claims as originally filed (or claims similar thereto), the Applicants have amended Claims 1-5 and 11-19. Specifically, Applicants have amended the preambles of these rejected claims, such that they now recite, "[a] method for producing recombinant mini-*Adenovirus* comprising" or "The method for producing recombinant mini-*Adenovirus* comprising." (emphasis added). In this respect, the claims now explicitly recite an intended outcome for the methods as claimed. The Applicants, therefore, respectfully request the Examiner withdraws this aspect (e.g. the form of the preamble) of the rejection under 35 U.S.C. §112 (second paragraph).

B. Vectors Are Definite

The Examiner states

"[c]laims 1, 12, 14 and 17 each recite a first vector followed by a step of culturing a cell transformed with the first vector in order to produce a second vector. The second vector can then be selected from a group of vectors comprising a third and fourth vector. The presence of the terms 'third vector' or 'fourth vector' imply that the third and fourth vectors are somehow distinct from the second vector. In fact, upon reading the specification it appears that the second vector is necessarily either the third or fourth vector. It would be remedial to amend the claim language by deleting the terms "third" and 'fourth' in referring to the different members of the Markush group of product vectors."²

Once again in order to further their business interests and without acquiescing to the Examiner's arguments, while expressly reserving the right to prosecute the claims as originally filed (or claims similar thereto), the Applicants have amended claims. Specifically, the claims that formerly recited a "a third vector" or "a fourth vector" now recite "a vector." Applicants submit that any ambiguity perceived by the Examiner is, hereby, remedied by this

¹ Office Action Mailed October 22, 2002, p. 3.

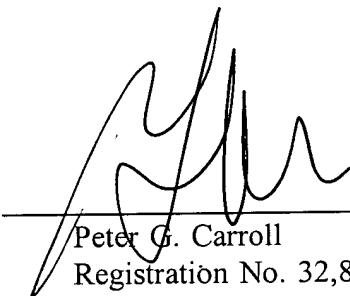
² *Id.*

amendment. The Applicants, therefore, respectfully request the Examiner withdraw this aspect of the rejection under 35 U.S.C. §112 (second paragraph).

CONCLUSION

Applicants believe that the arguments and amendments, set forth above, traverse the Examiner's rejections. Applicants, therefore, respectfully request these grounds for rejection be withdrawn and that the pending claims be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect at (617) 252-3353.

Dated: February 13, 2003



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APPENDIX I
MARKED-UP VERSION OF REWRITTEN, ADDED
AND/OR CANCELLED CLAIMS
PURSUANT TO 37 CFR § 1.121 (c)(1)(ii)

In the instant Response to the pending non-final Office Action, the claims were amended as follows:

IN THE CLAIMS:

1. (Amended) A method for producing recombinant mini-Adenovirus comprising:
 - a) providing:
 - i) a first recombinant vector, comprising in operable combination:
 - 1) a nucleotide sequence of interest having a 5' end and a 3' end;
 - 2) left and right inverted terminal repeats of adenovirus flanking said nucleotide sequence of interest;
 - 3) adenovirus packaging sequence linked to one of said inverted terminal repeats; and
 - 4) an adeno-associated virus terminal repeat sequence operably linked to said 3' end of said nucleotide sequence of interest,
wherein said first vector lacks a second adeno-associated virus terminal repeat sequence, and lacks one or more adenovirus early gene region selected from E1, E2, E3, and E4 gene region; and
 - ii) a cell capable of expressing said one or more adenovirus early gene which is lacking from said first vector;
 - b) introducing said first vector into said cell to produce a transformed cell; and
 - c) culturing said transformed cell under conditions such that a second vector is produced, said second vector selected from:

- i) a [third] vector, comprising in operable combination:
 - 1) adeno-associated virus terminal repeat[]-DD sequence;
 - 2) first and second inverted copies of a nucleotide sequence of interest flanking said adeno-associated virus terminal repeat-DD sequence;
 - 3) left and right inverted terminal repeats of adenovirus flanking said first and second inverted copies of said nucleotide sequence of interest; and
 - 4) an adenovirus packaging sequence linked to one of said inverted terminal repeats, and
- ii) a [fourth] vector, comprising in operable combination:
 - 1) a nucleotide sequence of interest having a 5' end and a 3' end;
 - 2) left and right inverted terminal repeats of adenovirus flanking said nucleotide sequence of interest; and
 - 3) an adenovirus packaging sequence linked to one of said inverted terminal repeats.

2. (Amended) The method for producing recombinant mini-Adenovirus of Claim 1, wherein said cell is capable of expressing one or more Rep proteins, and said culturing results in expression of said one or more Rep proteins.

3. (Amended) The method for producing recombinant mini-Adenovirus of Claim 1, wherein said second vector is encapsidated.

4. (Amended) The method for producing recombinant mini-Adenovirus of Claim 3, further comprising d) recovering said encapsidated second vector.

5. (Amended) The method for producing recombinant mini-Adenovirus of Claim 4, further comprising e) purifying said recovered encapsidated second vector.

11. (Amended) The method for producing recombinant mini-Adenovirus of Claim 2, wherein expression of one or more Rep proteins is inducible.

12. (Amended) A method for producing recombinant mini-Adenovirus comprising:

- a) providing:
 - i) a first recombinant vector, comprising in operable combination:
 - 1) a nucleotide sequence of interest having a 5' end and a 3' end;
 - 2) left and right inverted terminal repeats of adenovirus flanking said nucleotide sequence of interest;
 - 3) adenovirus packaging sequence linked to one of said inverted terminal repeats; and
 - 4) an adeno-associated virus terminal repeat sequence operably linked to said 3' end of said nucleotide sequence of interest,wherein said first vector lacks a second adeno-associated virus terminal repeat sequence, and lacks one or more adenovirus early gene region selected from E1, E2, and E4 gene region;
 - ii) a cell capable of expressing one or more Rep proteins; and
 - iii) helper adenovirus;
- b) introducing said first vector and genome of said helper adenovirus into said cell to produce a transformed cell; and
- c) culturing said transformed cell under conditions such that said transformed cell expresses said one or more Rep proteins, and a second vector is produced, said second vector selected from:

- i) a [third] vector, comprising in operable combination:
 - 1) adeno-associated virus terminal repeat[]-DD sequence;
 - 2) first and second inverted copies of a nucleotide sequence of interest flanking said adeno-associated virus terminal repeat-DD sequence;
 - 3) left and right inverted terminal repeats of adenovirus flanking said first and second inverted copies of said nucleotide sequence of interest; and
 - 4) an adenovirus packaging sequence linked to one of said inverted terminal repeats, and
- ii) a [fourth] vector, comprising in operable combination:
 - 1) a nucleotide sequence of interest having a 5' end and a 3' end;
 - 2) left and right inverted terminal repeats of adenovirus flanking said nucleotide sequence of interest; and
 - 3) an adenovirus packaging sequence linked to one of said inverted terminal repeats.

13. (Amended) The method for producing recombinant mini-Adenovirus of Claim 12, wherein said cell lacks expression of said one or more adenovirus early gene region which is lacking from said first vector.

14. (Amended) A method for producing recombinant mini-Adenovirus comprising:

- a) providing:
 - i) a first recombinant vector, comprising in operable combination:
 - 1) a nucleotide sequence of interest having a 5' end and a 3' end;

- 2) left and right inverted terminal repeats of adenovirus flanking said nucleotide sequence of interest;
- 3) adeno-associated virus terminal repeat sequence operably linked to said 3' end of said nucleotide sequence of interest,

wherein said first vector lacks a second adeno-associated virus terminal repeat sequence, and lacks one or more adenovirus early gene region selected from E1, E2, and E4 gene region;

 - ii) a cell capable of expressing said one or more adenovirus early gene region selected from E1, E2, and E4 gene region;
 - iii) a cell capable of expressing said one or more adenovirus early gene which is lacking from said first vector; and
 - iii) adeno-associated virus;
- b) introducing said first vector and genome of said adeno-associated virus into said cell to produce a transformed cell; and
- c) culturing said transformed cell under conditions such that a second vector is produced, said second vector selected from:
 - i) a [third] vector, comprising in operable combination:
 - 1) adeno-associated virus terminal repeat[]-DD sequence;
 - 2) first and second inverted copies of a nucleotide sequence of interest flanking said adeno-associated virus terminal repeat-DD sequence;
 - 3) left and right inverted terminal repeats of adenovirus flanking said first and second inverted copies of said nucleotide sequence of interest; and
 - 4) an adenovirus packaging sequence linked to one of said inverted terminal repeats, and
 - ii) a [fourth] vector, comprising in operable combination:
 - 1) a nucleotide sequence of interest having a 5' end and a 3' end;

- 2) left and right inverted terminal repeats of adenovirus flanking said nucleotide sequence of interest; and
- 3) an adenovirus packaging sequence linked to one of said inverted terminal repeats.

15. (Amended) A method for producing recombinant mini-Adenovirus comprising:

- a) providing:
 - i) a first recombinant vector, comprising in operable combination:
 - 1) a nucleotide sequence of interest having a 5' end and a 3' end;
 - 2) left and right inverted terminal repeats of adenovirus flanking said nucleotide sequence of interest;
 - 3) adenovirus packaging sequence linked to one of said inverted terminal repeats; and
 - 4) an adeno-associated virus terminal repeat sequence operably linked to said 3' end of said nucleotide sequence of interest,
wherein said first vector lacks a second adeno-associated virus terminal repeat sequence, and lacks adenovirus E3 early gene region; and
 - ii) a cell;
- b) introducing said first vector into said cell to produce a transformed cell; and
- c) culturing said transformed cell under conditions such that a second vector is produced, said second vector selected from:
 - i) a [third] vector, comprising in operable combination:
 - 1) adeno-associated virus terminal repeat[]-DD sequence;

- 2) first and second inverted copies of a nucleotide sequence of interest flanking said adeno-associated virus terminal repeat-DD sequence;
- 3) left and right inverted terminal repeats of adenovirus flanking said first and second inverted copies of said nucleotide sequence of interest; and
- 4) an adenovirus packaging sequence linked to one of said inverted terminal repeats, and

- ii) a [fourth] vector, comprising in operable combination:
 - 1) a nucleotide sequence of interest having a 5' end and a 3' end;
 - 2) left and right inverted terminal repeats of adenovirus flanking said nucleotide sequence of interest; and
 - 3) an adenovirus packaging sequence linked to one of said inverted terminal repeats.

16. (Amended) The method for producing recombinant mini-Adenovirus of Claim 15, wherein said cell is capable of expressing one or more of Rep proteins, and said culturing results in expression of said one or more Rep proteins.

17. (Amended) A method for producing recombinant mini-Adenovirus comprising:

- a) providing:
 - i) a first recombinant vector, comprising in operable combination:
 - 1) a nucleotide sequence of interest having a 5' end and a 3' end;
 - 2) left and right inverted terminal repeats of adenovirus flanking said nucleotide sequence of interest;
 - 3) adenovirus packaging sequence linked to one of

said inverted terminal repeats; and

- 4) an adeno-associated virus terminal repeat sequence operably linked to said 3' end of said nucleotide sequence of interest,

wherein said first vector lacks a second adeno-associated virus terminal repeat sequence, and wherein said nucleotide sequence of interest in said first vector comprises adeno-associated virus R[r]ep gene region; and

- ii) a cell;
- b) introducing said first vector into said cell to produce a transformed cell; and
- c) culturing said transformed cell under conditions such that said transformed cell expresses one or more Rep proteins, and a second vector is produced, said second vector selected from:
 - i) a [third] vector, comprising in operable combination:
 - 1) adeno-associated virus terminal repeat[]-DD sequence;
 - 2) first and second inverted pieces of a nucleotide sequence of interest flanking said adeno-associated virus terminal repeat-DD sequence;
 - 3) left and right inverted terminal repeats of adenovirus flanking said first and second inverted copies of said nucleotide sequence of interest; and
 - 4) an adenovirus packaging sequence linked to one of said inverted terminal repeats, and
 - ii) a [fourth] vector, comprising in operable combination:
 - 1) a nucleotide sequence of interest having a 5' end and a 3' end;
 - 2) left and right inverted terminal repeats of adenovirus flanking said nucleotide sequence of interest; and

3) an adenovirus packaging sequence linked to one of
said inverted terminal repeats.

18. (Amended) The method for producing recombinant mini-Adenovirus of
Claim 17, wherein said first vector lacks one or more adenovirus early gene region selected
from E1, E2, and E4 gene region, and said cell is capable of expressing said adenovirus early
gene region which is lacking from said first vector.

19. (Amended) The method for producing recombinant mini-Adenovirus of
Claim 17, wherein said first vector lacks adenovirus E3 gene region.